

What is claimed is:

1. An isolated and purified superantigen toxin DNA fragment which has been altered such that
5 binding of the encoded altered toxin to either the MHC class II or T cell antigen receptor is altered.
- 10 2. An isolated and purified DNA fragment according to claim 1, wherein said superantigen toxin is toxic shock syndrome toxin-1 having the sequence of SEQ ID NO:11 or a portion thereof, or an allelic portion thereof
- 15 3. An isolated and purified DNA fragment according to claim 1, wherein said superantigen toxin is Staphylococcal enterotoxin C1 having the sequence of SEQ ID NO:13 or a portion thereof, or an allelic portion thereof.
- 20 4. An isolated and purified DNA fragment according to claim 1, wherein said superantigen toxin is Streptococcal pyrogenic exotoxin A having the sequence of SEQ ID NO:15 or a portion thereof, or an allelic portion thereof.
- 25 5. An isolated and purified DNA fragment according to claim 1, wherein said superantigen toxin is toxic shock syndrome toxin-1 having the sequence of SEQ ID NO:11 or a portion thereof, or an allelic portion thereof further comprising a mutation wherein
30 said mutation results in a change in histidine 135 of said toxin from histidine to alanine.
- 35 6. An isolated and purified DNA fragment according to claim 1, wherein said superantigen is

Streptococcal pyrogenic exotoxin A fused to
Streptococcal pyrogenic exotoxin B, wherein said DNA
has the sequence of SEQ ID NO:23.

5 7. An isolated and purified DNA fragment
according to claim 2, wherein said fragment encodes
the amino acid sequence of SEQ ID NO:12 or a portion
thereof, or an allelic portion thereof.

10 8. An isolated and purified DNA fragment
according to claim 3, wherein said fragment encodes
the amino acid sequence of SEQ ID NO:14 or a portion
thereof, or an allelic portion thereof.

15 9. An isolated and purified DNA fragment
according to claim 4, wherein said fragment encodes
the amino acid sequence of SEQ ID NO:16 or a portion
thereof, or an allelic portion thereof.

20 10. An isolated and purified DNA fragment
according to claim 6, wherein said fragment encodes
the amino acid sequence of SEQ ID NO:27 or a portion
thereof, or an allelic portion thereof.

25 11. A recombinant DNA construct comprising:
 (i) a vector, and
 (ii) an isolated and purified altered
superantigen toxin DNA fragment according to claim 1.

30 12. A recombinant DNA construct according to
claim 11, wherein said DNA fragment has the sequence
according to SEQ ID NO:11 or a portion thereof, or an
allelic portion thereof.

13. A recombinant DNA construct according to claim 11, wherein said DNA fragment has the sequence according to SEQ ID NO:13 or a portion thereof, or an allelic portion thereof.

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14. A recombinant DNA construct according to claim 11, wherein said DNA fragment has the sequence according to SEQ ID NO:15 or a portion thereof, or an allelic portion thereof.

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15. A recombinant DNA construct according to claim 11, wherein said DNA fragment has the sequence according to SEQ ID NO:23 or a portion thereof, or an allelic portion thereof.

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16. The recombinant DNA construct according to claim 12, wherein said DNA fragment encodes the amino acid sequence specified in SEQ ID NO:12.

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17. The recombinant DNA construct according to claim 13, wherein said DNA fragment encodes the amino acid sequence specified in SEQ ID NO:14.

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18. The recombinant DNA construct according to claim 14, wherein said DNA fragment encodes the amino acid sequence specified in SEQ ID NO:16.

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19. The recombinant DNA construct according to claim 15, wherein said DNA fragment encodes the amino acid sequence specified in SEQ ID NO:27.

20. A recombinant DNA construct according to claim 16 wherein said construct is pETTST30.

21. A recombinant DNA construct according to
claim 17 wherein said construct is PETSEC45.

22. A recombinant DNA construct according to
5 claim 18 wherein said construct is PETSPEA42.

23. A recombinant DNA construct according to
claim 11, wherein said vector is an expression vector.

10 24. A host cell transformed with a
recombinant DNA construct according to claim 11.

25. A host cell transformed with a
recombinant construct according to claim 20.

15 26. A host cell transformed with a
recombinant construct according to claim 21.

20 27. A host cell transformed with a
recombinant construct according to claim 22.

25 28. A method for producing altered
superantigen toxin comprising culturing the cells
according to claim 24, under conditions such that said
DNA fragment is expressed and said superantigen toxin
is thereby produced, and isolating said superantigen
toxin.

30 29. A method for producing altered
superantigen toxin comprising culturing the cells
according to claim 25, under conditions such that said
DNA fragment is expressed and said superantigen toxin
is thereby produced, and isolating said superantigen
toxin.

30. A method for producing altered superantigen toxin comprising culturing the cells according to claim 26, under conditions such that said
5 DNA fragment is expressed and said superantigen toxin is thereby produced, and isolating said superantigen toxin.

31. A method for producing altered
10 superantigen toxin comprising culturing the cells according to claim 27, under conditions such that said DNA fragment is expressed and said superantigen toxin is thereby produced, and isolating said superantigen toxin.

15 32. An isolated and purified superantigen toxin which has been altered such that binding of the encoded altered toxin to either the MHC class II or T cell antigen receptor is altered.

20 33. An isolated and purified superantigen toxin according to claim 32 wherein said toxin is staphylococcal toxin shock syndrome toxin-1.

25 34. An isolated and purified superantigen toxin according to claim 32 wherein said toxin is staphylococcal enterotoxin C1.

30 35. An isolated and purified superantigen toxin according to claim 32 wherein said toxin is streptococcal pyrogenic exotoxin A.

35 36. An isolated and purified superantigen toxin according to claim 32 wherein said toxin is TSST-1.

37. An altered TSST-1 superantigen toxin peptide according to claim 36 wherein position 30 has been changed to alanine or arginine.

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38. An altered TSST-1 superantigen toxin peptide according to claim 36 wherein position 135 has been changed to alanine.

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39. An altered TSST-1 superantigen toxin peptide according to claim 36 wherein position 30 has been altered to arginine and position 135 has been altered to alanine.

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40. An altered SEC1 superantigen toxin peptide according to claim 34 wherein position 45 has been altered to lysine.

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41. An altered SpeA superantigen toxin peptide according to claim 35 wherein position 42 has been altered to alanine or arginine.

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42. An altered SpeA superantigen toxin according to claim 41 fused to an altered SpeB superantigen toxin peptide wherein said SpeB peptide position 47 has been altered to serine.

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43. The altered superantigen of claim 42 having amino acid SEQ ID NO:27.

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44. A method for the diagnosis of superantigen-associated bacterial infection comprising the steps of:
(i) contacting a sample from an individual suspected of having a superantigen-associated

bacterial infection with altered superantigen toxin;
and

- (ii) detecting the presence or absence of a superantigen-associated bacterial infection by
5 detecting the presence or absence of a complex formed between the altered superantigen toxin and antibodies specific therefor in the sample.

45. A method for the diagnosis of a
10 superantigen toxin-associated bacterial infection according to claim 40 wherein the altered superantigen toxin is chosen from the group consisting of SpeA, SEB, SEA, TSST-1, SEC-1.

15 46. A superantigen toxin-associated infection diagnostic kit comprising an altered superantigen toxin according to claim 32 wherein said toxin is chosen from the group consisting of SpeA, SEB, SEA, TSST-1, and SEC-1, and ancillary reagents
20 suitable for use in detecting the presence or absence of antibodies against superantigen toxin in a mammalian sample.

47. A vaccine comprising an altered
25 superantigen toxin according to claim 32 effective for the production of antigenic and immunogenic response resulting in the protection of a mammal against superantigen-associated bacterial infection.

30 48. A vaccine according to claim 47 wherein said altered superantigen toxin is chosen from the group consisting of SpeA, SEB, SEA, TSST-1, and SEC-1.

49. A vaccine according to claim 48 wherein said SpeA toxin further comprises an altered SpeB superantigen peptide.

5 50. A vaccine according to claim 48 wherein said vaccine further comprises at least one other different altered superantigen toxin chosen from the group consisting of SpeA, SEB, SEA, TSST-1, and SEC-1.

10 51. A multivalent vaccine against superantigen-associated bacterial infections comprising a combination of altered superantigen toxins selected from the group consisting essentially of TSST-1, SpeA , SEA, SEB, SEC-1, or any portion or 15 allelic form thereof, capable of eliciting protective antibodies against superantigen toxins in a pharmaceutically acceptable excipient in a pharmaceutically acceptable amount.

20 52. A multivalent vaccine according to claim 51 further comprising an altered SpeA superantigen or peptide thereof fused to an altered SpeB superantigen or peptide thereof.

25 53. A therapeutic method for the treatment or amelioration of a superantigen-associated bacterial infection said method comprising administering to an individual in need of such treatment an effective amount of sera from individuals immunized with one of 30 more altered superantigen toxin vaccine according to claim 47 in a pharmaceutically acceptable dose in a pharmaceutically acceptable excipient.

35 54. A therapeutic method for the treatment or amelioration of a superantigen-associated bacterial

infection, said method comprising administering to an individual in need of such treatment an effective amount of antibodies against altered superantigen toxins in a pharmaceutically acceptable dose in a 5 pharmaceutically acceptable excipient.

55. A therapeutic method for the treatment or amelioration of a superantigen-associated bacterial infection, said method comprising administering to an 10 individual in need of such treatment an effective amount of altered superantigen toxins from streptococcal and staphylococcal bacteria in order to inhibit adhesion of superantigen bacterial toxin to MHC class II or T cell receptors by competitive inhibition 15 of these interactions in a pharmaceutically acceptable dose in a pharmaceutically acceptable excipient.

56. A therapeutic method for the treatment of diseases that may not be associated directly with 20 superantigen toxins by causing specific nonresponsiveness of T cell subsets or by expanding or stimulating specific T cell subsets, *in vivo* or *ex vivo* by use of altered superantigen toxin.

25 57. Antisera isolated from individuals immunized with one or more altered TSST-1 superantigen toxin.

30 58. Antisera according to claim 57 wherein said altered superantigen toxin TSST-1 comprises TSST-1 wherein position 30 has been altered to arginine or alanine.

35 59. Antisera according to claim 57 wherein said altered superantigen toxin TSST-1 comprises TSST-

1 wherein position 30 has been altered to arginine or
alanine and position 135 has been altered to alanine.

5 60. Antisera according to claim 57 wherein
said altered superantigen toxin is SEC1.

61. Antisera according to claim 60 wherein
said SEC1 position 45 has been altered to lysine.

10 62. Antisera according to claim 57 wherein
said altered superantigen toxin is SpeA.

63. Antisera according to claim 62 wherein
said SpeA position 42 has been altered to alanine.

15 64. Antisera according to claim 62 wherein
said SpeA position 42 has been altered to arginine.

20 65. Antisera according to claim 57 wherein
said altered superantigen toxin is SpeA wherein said
SpeA position 42 has been altered to alanine, and said
SpeA fused to an altered SpeB superantigen toxin
wherein said SpeB position 47 has been altered to
serine.

25 66. An antibody which recognizes altered
TSST-1.

30 67. An antibody according to claim 66
wherein said TSST-1 comprises a change to arginine at
position 30.

35 68. An antibody according to claim 66
wherein said TSST-1 comprises a change to alanine at
position 30.

69. An antibody which recognizes altered SEC1.

5 70. An antibody according to claim 69 wherein said SEC-1 comprises a change to lysine at position 45.

10 71. An antibody which recognizes altered SpeA.

15 72. An antibody according to claim 71 wherein said SpeA comprises a change to alanine at position 42.

20 73. An antibody according to claim 71 wherein said SpeA comprises a change to arginine at position 42.

25 74. An antibody according to claim 71 wherein said SpeA comprises a change to alanine at position 42 and is fused to an altered SpeB wherein said SpeB comprises a change to serine at position 47.

30 75. An antibody according to claim 71 wherein said SpeA comprises a change to arginine at position 42 and is fused to an altered SpeB wherein said SpeB comprises a change to serine at position 47.

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